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Mining transcriptome data to identify consequential microRNAs and their targets

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Although microRNAs (miRNAs) contribute to essentially all mammalian gene regulatory pathways, the identification of consequential miRNAs active in a given cell-type remains challenging. To address this challenge, mRNA and miRNA transcriptome profiles can be used to infer the identities of miRNAs with regulatory impacts. We used such approaches to discover miRNAs that might underlie age-dependent differences in CD8+ T cells, which protect organisms from intracellular diseases. In early life, mice and other mammals are deficient at generating memory CD8+ T cells, which protect from re-infection; we hypothesized that age-specific activity of one or more miRNAs underlie these differences. We profiled mouse transcriptomes from CD8+ T cells at different stages of infection, comparing adult and neonatal profiles. Adult and neonatal miRNA profiles were surprisingly similar in effector cell populations created during infection; however, we observed large differences prior to infection; in particular, miR-29 and miR-130 exhibit significant differential expression between adult and neonatal naive cells. Importantly, we detected reciprocal changes in expression of mRNA targets for both miRNAs; moreover, targets include Eomes and Tbx21, key genes that regulate memory CD8+ T cell formation. In addition, the mRNA profiles of neonatal naive cells already resemble those of effector cells. Changes in miR-29 and miR-130 and their targets are conserved in human CD8+ T cells, and in other T cell lineages. Together, these results suggest that miR-29 and miR-130 are important regulators of memory CD8+ T cell formation, and that neonatal cells are committed to a short-lived effector cell fate prior to infection.

Biography

Andrew Grimson has completed his PhD at the University of Wisconsin-Madison in 2004, investigating mRNA decay. He completed his Post-doctoral fellowship in 2009, mentored by Dr. David Bartel (Whitehead Institute/MIT), investigating microRNAs and their targets. Currently, he is an Assistant Professor of Molecular Biology and Genetics at Cornell University. His lab work is on post-transcriptional regulation, in particular the role of the 3′ untranslated region (3′UTR); research is focused upon the basic science of 3′UTRs, together with biological processes under post-transcriptional control. His research is supported by grants from the NIH, and by a Research Scholar Grant from the American Cancer Society.

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